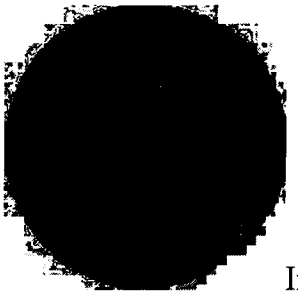
EXHIBIT 3

REDACTED IN ITS ENTIRETY

EXHIBIT 4



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    - As stated above, once you are in the HTML patent list, you will notice that a series of the patent 'Document Numbers' are highlighted in blue and are underlined. This indicates that the is a text version of this patent. Double click on the 'Document Number' to view the text. Note: If you are using MS Internet Explorer 4+, this may open the text in the browser; use 'Back' to return to the list of patents.

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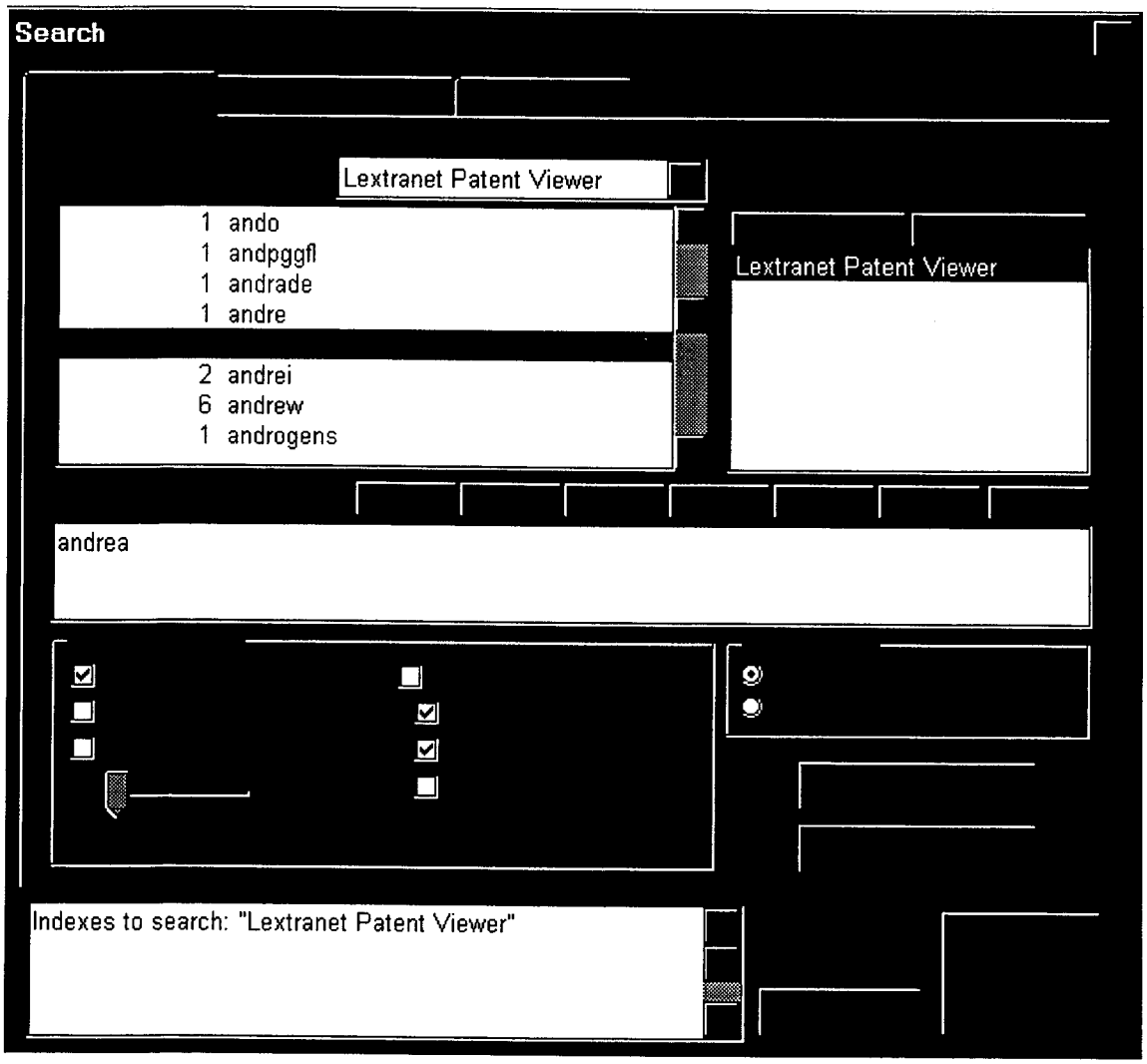
Once the program is running, you can start your search by clicking on the 'Search' icon (the second from the left on the toolbar). When you click on it you will see the 'Search' Window as seen below:



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The search will open the first document with the first occurrence of the search. You may view the document either within dtSearch program itself (ordinary typewriter-style fonts, and no graphics), or in its original HTML format with hyperlinks to the image files. To view the HTML file in your browser, click the Launch button on the dtSearch toolbar. Return to dtSearch from the document by clicking on the dtSearch icon on your task bar to view the full list of 'hits'.

Note that there may be multiple 'hits' or matches of your search terms, so you may browse to many different patents for viewing.

EXHIBIT 5

COPY

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PHARMACEUTICALS, INC.

IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF CALIFORNIA
SAN FRANCISCO

AFFYMETRIX, INC., Plaintiff and counterdefendant, v. SYNTENI, INC. and INCYTE PHARMACEUTICALS, INC., Defendants and counterplaintiffs.	Case No. C98-4508 FMS (MEJ) **INITIAL DISCLOSURE OF PRIOR ART PURSUANT TO 16-7**

In accordance with Civil L.R. 16-7, Defendants Incyte Pharmaceuticals, Inc. and Synteni, Inc., hereby submit this initial disclosure of prior art developed to date relating to U.S. Patent No. 5,744,305 ('305 Patent). Defendants are actively engaged in searching out other prior art and persons working in the technologies to which the '305 patent relates. Defendants anticipate that such effort may yield additional prior art of comparable relevance to what is disclosed below, and defendants intend to supplement this disclosure as such additional prior art is located.

Prior Art Affecting the Validity of U.S. Patent No. 5,744,305

Defendants' investigation to date has resulted in the identification of the following prior art references that appear, on their face, to anticipate or render obvious Claims 1-13 and 15-25 of the '305 Patent. Defendants acknowledge that numerous disputed issues of claim construction may lie ahead, altering significantly the manner in which a determination of patent validity under 35 U.S.C. §§ 102 and 103 would be carried out. Defendants also acknowledge that issues of enablement may affect the scope or relevance of certain prior art. Defendants have accepted the disclosed prior art at face value and have made no attempt, at this preliminary stage, to evaluate the future impact of claim construction and enablement issues that may be presented.

The asserted claims 1-13 and 15-25 of the '305 patent when interpreted as broadly as Affymetrix appears to be interpreting them, are invalid under 35 U.S.C. §102 as anticipated by, or under 35 U.S.C. §103 as obvious in view of, the following prior art references.

1. Claims 1-13 and 15-25 of the '305 patent are anticipated by Hanahan *et al.* "Plasmid Screening at High Colony Density", Methods in Enzymology 100:333-342 (1983), or obvious in light of Hanahan *et al.* in combination with Arnold, Jr., US 5,362,866 (11/94), Damagupta et al., EP 0 281 927 A2 (9/88), Frank, *et al.*, "Simultaneous Synthesis and Biological Applications of DNA Fragments: An Efficient and Complete Methodology," Methods in Enzymology 134:221-251 (1987), Groet, *et al.*, US 4,533,682 (5/86), Guire, US 4,973,493 (11/90), Macevicz, US 5,002,867 (5/91), Southern and Maskos, WO 90/03382 (4/90), Urdea et al, US 4,517,338 (5/85), Damagupta et al., US 5,348,855 (9/94), Drmanac et al., US 5,202,231 (8/93), Eggers, *et al.*, US 5,532,128 (7/96), Erlich et al., EP 0 237 362 B1 (9/87), Khrapko et al., "An Oligonucleotide Hybridization Approach to DNA Sequencing," FEB 256:118-122 (1989), Khrapko et al., "Hybridization of DNA with Oligonucleotides Immobilized in Gel," Molecular Biology 25:581-591 (1991), Lysov et al., "A New Method For Determining the DNA Nucleotide Sequence By Hybridization With Oligonucleotides," Doklady Biochemistry 303:355-452 (1988), Palva et al., GB 2 156 074A (10/85), Potter, US 4,613,566 (9/86), Saiki and Erlich, WO 89/11548 (11/89), Southern, US 5,700,637 (12/97), Southern, WO 89/10977 (11/89), and/or Wang et al., US 4,925,785 (5/90).

2. Claims 1-13 and 15-25 of the '305 parent are anticipated by Southern USP 5,700,637 (12/97), or obvious in light of Southern in combination with Cozzette et al., US 5,200,051 (4/93), Hayes et al., US 4,877,745 (10/89), Kimura et al., "An Immobilized Enzyme Membrane Fabrication Method Using an Ink Jet Nozzle," Biosensors 40:41-52 (1988), Kuriyama, JP Sho 63-223557 (9/88), Miyagi et al., JP 59-24244 (2/84), Madou et al., US 4,874,500 (10/89), Arnold, Jr., US 5,362,866 (11/94), Dattagupta et al., EP 0 281 927 A2 (9/88), Frank, *et al.*, "Simultaneous Synthesis and Biological Applications of DNA Fragments: An Efficient and Complete Methodology," Methods in Enzymology 134:221-251 (1987), Groet, *et al.*, US 4,533,682 (5/86), Guire, US 4,973,493 (11/90), Macevicz, US 5,002,867 (5/91), Southern and Maskos, WO 90/03382 (4/90), Urdea et al, US 4,517,338 (5/85), Dattagupta et al., US 5,348,855 (9/94), Drmanac et al., US 5,202,231 (8/93), Eggers, *et al.*, US 5,532,128 (7/96), Erlich et al., EP 0 237 362 B1 (9/87), Khrapko et al., "An Oligonucleotide Hybridization Approach to DNA Sequencing," FEB 256:118-122 (1989), Khrapko et al., "Hybridization of DNA with Oligonucleotides Immobilized in Gel," Molecular Biology 25:581-591 (1991), Lysov et al., "A New Method For Determining the DNA Nucleotide Sequence By Hybridization With Oligonucleotides," Doklady Biochemistry 303:355-452 (1988), Palva et al., GB 2 156 074A (10/85), Power, US 4,613,566 (9/86), Saiki and Erlich, WO 89/11548 (11/89), Southern, WO 89/10977 (11/89) and/or Wang et al., US 4,925,785 (5/90).

3. Claims 1-13 and 15-25 of the '305 patent are anticipated by Southern WO 89/10977, or obvious in light of Southern in combination with Cozzette et al., US 5,200,051 (4/93), Hayes et al., US 4,877,745 (10/89), Kimura et al., "An Immobilized Enzyme Membrane Fabrication Method Using an Ink Jet Nozzle," Biosensors 40:41-52 (1988), Kuriyama, JP Sho 63-223557 (9/88), Miyagi et al., JP 59-24244 (2/84), Madou et al., US 4,874,500 (10/89), Arnold, Jr., US 5,362,866 (11/94), Dattagupta et al., EP 0 281 927 A2 (9/88), Frank, *et al.*, "Simultaneous Synthesis and Biological Applications of DNA Fragments: An Efficient and Complete Methodology," Methods in Enzymology 134:221-251 (1987), Groet, *et al.*, US 4,533,682 (5/86), Guire, US 4,973,493 (11/90), Macevicz, US 5,002,867 (5/91), Southern and Maskos, WO 90/03382 (4/90), Urdea et al, US 4,517,338 (5/85), Dattagupta et al., US 5,348,855 (9/94), Drmanac et al., US 5,202,231 (8/93), Eggers, *et al.*, US 5,532,128 (7/96), Erlich et al., EP 0 237 362 B1 (9/87), Khrapko et al., "An

Oligonucleotide Hybridization Approach to DNA Sequencing," FEB 256:118-122 (1989), Khrapko et al., "Hybridization of DNA with Oligonucleotides Immobilized in Gel," Molecular Biology 25:581-591 (1991), Lysov et al., "A New Method For Determining the DNA Nucleotide Sequence By Hybridization With Oligonucleotides," Doklady Biochemistry 303:355-452 (1988), Palva et al., GB 2 156 074A (10/85), Potter, US 4,613,566 (9/86), Saiki and Erlich, WO 89/11548 (11/89), Southern, US 5,700,637 (12/97), and/or Wang et al., US 4,925,785 (5/90).

4. Claims 1-13 and 15-25 of the '305 patent are anticipated by Eggers *et al* USP 5,532,128 (7/96), or obvious in light of Eggers in combination with Cozzette et al., US 5,200,051 (4/93), Hayes et al., US 4,877,745 (10/89), Kimura et al., "An Immobilized Enzyme Membrane Fabrication Method Using an Ink Jet Nozzle," Biosensors 40:41-52 (1988), Kuriyama, JP Sho 63-223557 (9/88), Miyagi et al., JP 59-24244 (2/84), Madou et al., US 4,874,500 (10/89), Arnold, Jr., US 5,362,866 (11/94), Damagupta et al., EP 0 281 927 A2 (9/88), Frank, *et al.*, "Simultaneous Synthesis and Biological Applications of DNA Fragments: An Efficient and Complete Methodology," Methods in Enzymology 134:221-251 (1987), Groet, *et al.*, US 4,533,682 (5/86), Guire, US 4,973,493 (11/90), Macevicz, US 5,002,867 (5/91), Southern and Maskos, WO 90/03382 (4/90), Urdea et al, US 4,517,338 (5/85), Damagupta et al., US 5,348,855 (9/94), Drmanac et al., US 5,202,231 (8/93), Erlich et al., EP 0 237 362 B1 (9/87), Khrapko et al., "An Oligonucleotide Hybridization Approach to DNA Sequencing," FEB 256:118-122 (1989), Khrapko et al., "Hybridization of DNA with Oligonucleotides Immobilized in Gel," Molecular Biology 25:581-591 (1991), Lysov et al., "A New Method For Determining the DNA Nucleotide Sequence By Hybridization With Oligonucleotides," Doklady Biochemistry 303:355-452 (1988), Palva et al., GB 2 156 074A (10/85), Potter, US 4,613,566 (9/86), Saiki and Erlich, WO 89/11548 (11/89), Southern, US 5,700,637 (12/97), Southern, WO 89/10977 (11/89), and/or Wang et al., US 4,925,785 (5/90).

5. Claims 1-13 and 15-25 of the '305 patent are anticipated by Khrapko et al., "An Oligonucleotide Hybridization Approach to DNA Sequencing," FEB 256:118-122 (1989), or obvious in light of Khrapko in combination with Cozzette et al., US 5,200,051 (4/93), Hayes et al., US 4,877,745 (10/89), Kimura et al., "An Immobilized Enzyme

Membrane Fabrication Method Using an Ink Jet Nozzle," Biosensors 40:41-52 (1988), Kuriyama, JP Sho 63-223557 (9/88), Miyagi et al., JP 59-24244 (2/84), Madou et al., US 4,874,500 (10/89), Arnold, Jr., US 5,362,866 (11/94), Dattagupta et al., EP 0 281 927 A2 (9/88), Frank, *et al.*, "Simultaneous Synthesis and Biological Applications of DNA Fragments: An Efficient and Complete Methodology," Methods in Enzymology 134:221-251 (1987), Groet, *et al.*, US 4,533,682 (5/86), Guire, US 4,973,493 (11/90), Macevicz, US 5,002,867 (5/91), Southern and Maskos, WO 90/03382 (4/90), Urdea et al, US 4,517,338 (5/85), Dattagupta et al., US 5,348,855 (9/94), Drmanac et al., US 5,202,231 (8/93), Eggers, *et al.*, US 5,532,128 (7/96), Erlich et al., EP 0 237 362 B1 (9/87), Khrapko et al., "Hybridization of DNA with Oligonucleotides Immobilized in Gel," Molecular Biology 25:581-591 (1991), Lysov et al., "A New Method For Determining the DNA Nucleotide Sequence By Hybridization With Oligonucleotides," Doklady Biochemistry 303:355-452 (1988), Palva et al., GB 2 156 074A (10/85), Potter, US 4,613,566 (9/86), Saiki and Erlich, WO 89/11548 (11/89), Southern, US 5,700,637 (12/97), Southern, WO 89/10977 (11/89), and/or Wang et al., US 4,925,785 (5/90).

6. Claims 1-13 and 15-25 of the '305 patent are anticipated by Drmanac et al., US 5,202,231 (8/93), or obvious in light of Drmanac in combination with Cozzette et al., US 5,200,051 (4/93), Hayes et al., US 4,877,745 (10/89), Kimura et al., "An Immobilized Enzyme Membrane Fabrication Method Using an Ink Jet Nozzle," Biosensors 40:41-52 (1988), Kuriyama, JP Sho 63-223557 (9/88), Miyagi et al., JP 59-24244 (2/84), Madou et al., US 4,874,500 (10/89), Arnold, Jr., US 5,362,866 (11/94), Dattagupta et al., EP 0 281 927 A2 (9/88), Frank, *et al.*, "Simultaneous Synthesis and Biological Applications of DNA Fragments: An Efficient and Complete Methodology," Methods in Enzymology 134:221-251 (1987), Groet, *et al.*, US 4,533,682 (5/86), Guire, US 4,973,493 (11/90), Macevicz, US 5,002,867 (5/91), Southern and Maskos, WO 90/03382 (4/90), Urdea et al, US 4,517,338 (5/85), Dattagupta et al., US 5,348,855 (9/94), Khrapko et al., "An Oligonucleotide Hybridization Approach to DNA Sequencing," FEB 256:118-122 (1989), Eggers, *et al.*, US 5,532,128 (7/96), Erlich et al., EP 0 237 362 B1 (9/87), Khrapko et al., "Hybridization of DNA with Oligonucleotides Immobilized in Gel," Molecular Biology 25:581-591 (1991), Lysov et al., "A New Method For Determining the DNA Nucleotide Sequence By Hybridization With Oligonucleotides," Doklady

Biochemistry 303:355-452 (1988), Palva et al., GB 2 156 074A (10/85), Potter, US 4,613,566 (9/86), Saiki and Erlich, WO 89/11548 (11/89), Southern, US 5,700,637 (12/97), Southern, WO 89/10977 (11/89), and/or Wang et al., US 4,925,785 (5/90).

7. Claims 1-13 and 15-25 of the '305 patent are anticipated by Drmanac et al., Yugoslav Patent No. 570/87 (2/88), or obvious in light of Drmanac in combination with Cozzette et al., US 5,200,051 (4/93), Hayes et al., US 4,877,745 (10/89), Kimura et al., "An Immobilized Enzyme Membrane Fabrication Method Using an Ink Jet Nozzle," Biosensors 40:41-52 (1988), Kuriyama, JP Sho 63-223557 (9/88), Miyagi et al., JP 59-24244 (2/84), Madou et al., US 4,874,500 (10/89), Arnold, Jr., US 5,362,866 (11/94), Damagupta et al., EP 0 281 927 A2 (9/88), Frank, *et al.*, "Simultaneous Synthesis and Biological Applications of DNA Fragments: An Efficient and Complete Methodology," Methods in Enzymology 134:221-251 (1987), Groet, *et al.*, US 4,533,682 (5/86), Guire, US 4,973,493 (11/90), Macevicz, US 5,002,867 (5/91), Southern and Maskos, WO 90/03382 (4/90), Urdea et al, US 4,517,338 (5/85), Damagupta et al., US 5,348,855 (9/94), Khrapko et al., "An Oligonucleotide Hybridization Approach to DNA Sequencing," FEB 256:118-122 (1989), Eggers, *et al.*, US 5,532,128 (7/96), Erlich et al., EP 0 237 362 B1 (9/87), Khrapko et al., "Hybridization of DNA with Oligonucleotides Immobilized in Gel," Molecular Biology 25:581-591 (1991), Lysov et al., "A New Method For Determining the DNA Nucleotide Sequence By Hybridization With Oligonucleotides," Doklady Biochemistry 303:355-452 (1988), Palva et al., GB 2 156 074A (10/85), Potter, US 4,613,566 (9/86), Saiki and Erlich, WO 89/11548 (11/89), Southern, US 5,700,637 (12/97), Southern, WO 89/10977 (11/89), and/or Wang et al., US 4,925,785 (5/90).

8. Claims 1-13 and 15-25 of the '305 patent are anticipated by Lysov et al., "A New Method For Determining the DNA Nucleotide Sequence By Hybridization With Oligonucleotides," Doklady Biochemistry 303:355-452 (1988) or obvious in light of Lysov in combination with Cozzette et al., US 5,200,051 (4/93), Hayes et al., US 4,877,745 (10/89), Kimura et al., "An Immobilized Enzyme Membrane Fabrication Method Using an Ink Jet Nozzle," Biosensors 40:41-52 (1988), Kuriyama, JP Sho 63-223557 (9/88), Miyagi et al., JP 59-24244 (2/84), Madou et al., US 4,874,500 (10/89),

Arnold, Jr., US 5,362,866 (11/94), Damagupta et al., EP 0 281 927 A2 (9/88), Frank, *et al.*, "Simultaneous Synthesis and Biological Applications of DNA Fragments: An Efficient and Complete Methodology," Methods in Enzymology 134:221-251 (1987), Groet, *et al.*, US 4,533,682 (5/86), Guire, US 4,973,493 (11/90), Macevicz, US 5,002,867 (5/91), Southern and Maskos, WO 90/03382 (4/90), Urdea et al, US 4,517,338 (5/85), Damagupta et al., US 5,348,855 (9/94), Drmanac et al., US 5,202,231 (8/93), Eggers, *et al.*, US 5,532,128 (7/96), Erlich et al., EP 0 237 362 B1 (9/87), Khrapko et al., "Hybridization of DNA with Oligonucleotides Immobilized in Gel," Molecular Biology 25:581-591 (1991), Palva et al., GB 2 156 074A (10/85), Potter, US 4,613,566 (9/86), Saiki and Erlich, WO 89/11548 (11/89), Southern, US 5,700,637 (12/97), Southern, WO 89/10977 (11/89), and/or Wang et al., US 4,925,785 (5/90).

9. Claims 1-13 and 15-25 of the '305 parent are rendered obvious under 35 U.S.C. 103 in view of Damagupta et al., US 5,348,855 (9/94) in combination with Cozzette et al., US 5,200,051 (4/93), Hayes et al., US 4,877,745 (10/89), Kimura et al., "An Immobilized Enzyme Membrane Fabrication Method Using an Ink Jet Nozzle," Biosensors 40:41-52 (1988), Kuriyama, JP Sho 63-223557 (9/88), Miyagi et al., JP 59-24244 (2/84), Madou et al., US 4,874,500 (10/89), Chang, US 4,591,570 (5/86), Chang, WO 84/03151 (8/84), Clark et al., US 4,728,591 (5/88), Cozzette et al., US 5,200,051 (4/93), Ekins, "Developments In Immunoassay Methods," Biochimica Clinica Suppl. 1/8:13 (1989), Ekins, US 5,432,099 (11/95), Ekins et al., "Fluorescence Spectroscopy and its Application to a New Generation of High Sensitivity, Multi-Microspot, Multianalyte, Immunoassay," Clinica Chimica Acta 194:91-114 (1990), Geysen, WO 84/03564 (9/84), Gordon et al., EP 0 063 810 A1 (11/82), Herzberg and Fish, EP 0 171 150 B1 (2/86), Huang, US 4,327,073 (4/82), Humphries et al., US 4,704,353 (11/87), Johnson, US 4,216,245 (8/80), Kleinfeld et al., "Controlled Outgrowth of Dissociated Neurons on Patterned Substrates," J. Neuroscience 8:4098-4120 (1988), Lowe and Earley, US 4,562,157 (12/85), Madou et al., US 4,874,500 (10/89), Drmanac et al., US 5,202,231 (8/93), Eggers, *et al.*, US 5,532,128 (7/96), Erlich et al., EP 0 237 362 B1 (9/87), Khrapko et al., "An Oligonucleotide Hybridization Approach to DNA Sequencing," FEB 256:118-122 (1989), Khrapko et al., "Hybridization of DNA with Oligonucleotides Immobilized in Gel," Molecular Biology 25:581-591 (1991), Lysov et al., "A New

Method For Determining the DNA Nucleotide Sequence By Hybridization With Oligonucleotides," Doklady Biochemistry 303:355-452 (1988), Palva et al., GB 2 156 074A (10/85), Potter, US 4,613,566 (9/86), Saiki and Erlich, WO 89/11548 (11/89), Southern, US 5,700,637 (12/97), Southern, WO 89/10977 (11/89), and/or Wang et al., US 4,925,785 (5/90).

10. Claims 1-13 and 15-25 of the '305 patent are rendered obvious under 35 U.S.C. 103 in view of Wang et al., US 4,925,785 (5/90) in combination with Cozzette et al., US 5,200,051 (4/93), Hayes et al., US 4,877,745 (10/89), Kimura et al., "An Immobilized Enzyme Membrane Fabrication Method Using an Ink Jet Nozzle," Biosensors 40:41-52 (1988), Kuriyama, JP Sho 63-223557 (9/88), Miyagi et al., JP 59-24244 (2/84), Madou et al., US 4,874,500 (10/89), Chang, US 4,591,570 (5/86), Chang, WO 84/03151 (8/84), Clark et al., US 4,728,591 (5/88), Cozzette et al., US 5,200,051 (4/93), Ekins, "Developments In Immunoassay Methods," Biochimica Clinica Suppl. 1/8:13 (1989), Ekins, US 5,432,099 (11/95), Ekins et al., "Fluorescence Spectroscopy and its Application to a New Generation of High Sensitivity, Multi-Microspot, Multianalyte, Immunoassay," Clinica Chimica Acta 194:91-114 (1990), Geysen, WO 84/03564 (9/84), Gordon et al., EP 0 063 810 A1 (11/82), Herzberg and Fish, EP 0 171 150 B1 (2/86), Huang, US 4,327,073 (4/82), Humphries et al., US 4,704,353 (11/87), Johnson, US 4,216,245 (8/80), Kleinfeld et al., "Controlled Outgrowth of Dissociated Neurons on Patterned Substrates," J. Neuroscience 8:4098-4120 (1988), Lowe and Earley, US 4,562,157 (12/85), Madou et al., US 4,874,500 (10/89), Dreamac et al., US 5,202,231 (8/93), Eggers, *et al.*, US 5,532,128 (7/96), Erlich et al., EP 0 237 362 B1 (9/87), Khrapko et al., "An Oligonucleotide Hybridization Approach to DNA Sequencing," FEB 256:118-122 (1989), Khrapko et al., "Hybridization of DNA with Oligonucleotides Immobilized in Gel," Molecular Biology 25:581-591 (1991), Lysov et al., "A New Method For Determining the DNA Nucleotide Sequence By Hybridization With Oligonucleotides," Doklady Biochemistry 303:355-452 (1988), Palva et al., GB 2 156 074A (10/85), Potter, US 4,613,566 (9/86), Saiki and Erlich, WO 89/11548 (11/89), Southern, US 5,700,637 (12/97), Southern, WO 89/10977 (11/89), and/or Dattagupta et al., US 5,348,855 (9/94).

11. Claims 1-13 and 15-25 of the '305 patent are rendered obvious under 35 U.S.C. 103 in view of Saiki *et al.*, "Genetic analysis of amplified DNA with immobilized sequence-specific oligonucleotide probes", *Proc. Natl. Acad. Sci. USA*, 86:6230-6234 (1989), in combination with Cozzette et al., US 5,200,051 (4/93), Hayes et al., US 4,877,745 (10/89), Kimura et al., "An Immobilized Enzyme Membrane Fabrication Method Using an Ink Jet Nozzle," Biosensors 40:41-52 (1988), Kuriyama, JP Sho 63-223557 (9/88), Miyagi et al., JP 59-24244 (2/84), Madou et al., US 4,874,500 (10/89), Chang, US 4,591,570 (5/86), Chang, WO 84/03151 (8/84), Clark et al., US 4,728,591 (5/88), Cozzette et al., US 5,200,051 (4/93), Ekins, "Developments In Immunoassay Methods," Biochimica Clinica Suppl. 1/8:13 (1989), Ekins, US 5,432,099 (11/95), Ekins et al., "Fluorescence Spectroscopy and its Application to a New Generation of High Sensitivity, Multi-Microspot, Multianalyte, Immunoassay," Clinica Chimica Acta 194:91-114 (1990), Geysen, WO 84/03564 (9/84), Gordon et al., EP 0 063 810 A1 (11/82), Herzberg and Fish, EP 0 171 150 B1 (2/86), Huang, US 4,327,073 (4/82), Humphries et al., US 4,704,353 (11/87), Johnson, US 4,216,245 (8/80), Kleinfeld et al., "Controlled Outgrowth of Dissociated Neurons on Patterned Substrates," J. Neuroscience 8:4098-4120 (1988), Lowe and Earley, US 4,562,157 (12/85), Madou et al., US 4,874,500 (10/89), Dimanac et al., US 5,202,231 (8/93), Eggers, *et al.*, US 5,532,128 (7/96), Erlich et al., EP 0 237 362 B1 (9/87), Khrapko et al., "An Oligonucleotide Hybridization Approach to DNA Sequencing," FEB 256:118-122 (1989), Khrapko et al., "Hybridization of DNA with Oligonucleotides Immobilized in Gel," Molecular Biology 25:581-591 (1991), Lysov et al., "A New Method For Determining the DNA Nucleotide Sequence By Hybridization With Oligonucleotides," Doklady Biochemistry 303:355-452 (1988), Palva et al., GB 2 156 074A (10/85), Power, US 4,613,566 (9/86), Saiki and Erlich, WO 89/11548 (11/89), Southern, US 5,700,637 (12/97), Southern, WO 89/10977 (11/89), and/or Wang et al., US 4,925,785 (5/90).

12. Claims 1-13 and 15-25 of the '305 patent are rendered obvious under 35 U.S.C. 103 in view of Humphries et al., US 4,704,353 (11/87) in combination with Damagupta et al., US 5,348,855 (9/94), Dimanac et al., US 5,202,231 (8/93), Eggers, *et al.*, US 5,532,128 (7/96), Erlich et al., EP 0 237 362 B1 (9/87), Khrapko et al., "An Oligonucleotide Hybridization Approach to DNA Sequencing," FEB 256:118-122 (1989), Khrapko et al.,

"Hybridization of DNA with Oligonucleotides Immobilized in Gel," Molecular Biology 25:581-591 (1991), Lysov et al., "A New Method For Determining the DNA Nucleotide Sequence By Hybridization With Oligonucleotides," Doklady Biochemistry 303:355-452 (1988), Palva et al., GB 2 156 074A (10/85), Porter, US 4,613,566 (9/86), Saiki and Erlich, WO 89/11548 (11/89), Southern, US 5,700,637 (12/97), Southern, WO 89/10977 (11/89), Wang et al., US 4,925,785 (5/90), Arnold, Jr., US 5,362,866 (11/94), Dattagupta et al., EP 0 281 927 A2 (9/88), Frank, *et al.*, "Simultaneous Synthesis and Biological Applications of DNA Fragments: An Efficient and Complete Methodology," Methods in Enzymology 134:221-251 (1987), Groet, *et al.*, US 4,533,682 (5/86), Guire, US 4,973,493 (11/90), Macevicz, US 5,002,867 (5/91), Southern and Maskos, WO 90/03382 (4/90), Urdea et al, US 4,517,338 (5/85), Augenlicht, US 4,981,783 (1/91), Craig et al., "Ordering of Cosmid Clones Covering the Herpes Simplex Virus Type I (HSV-I)" Genome, Nuc. Acids. Res. 18:2653-2660 (1990), Gergen et al., "Filter Replicas and Permanent Collections of Recombinant DNA Plasmids," Nucleic Acids Res. 7:2115-2135 (1979), Gillespie, *et al.*, US 4,483,920, (11/84), Hanahan & Meselson, "Plasmid Screening at High Colony Density," Gene 10:63-67, (1980), Hanahan & Meselson, "Plasmid Screening at High Colony Density," Methods in Enzymology 100:333-342, (1983), Kohara *et al.*, "The Physical Map of the Whole E. coli Chromosome: Application of a New Strategy for Rapid Analysis and Sorting of a Large Genomic Library," Cell 50: 495-508 (1987), and/or White *et al.*, US 4,677,054 (6/87).

13. Claims 1-13 and 15-25 of the '305 patent are rendered obvious under 35 U.S.C. 103 in view of Augenlicht, US 4,981,783 (1/91) in combination with Cozzette et al., US 5,200,051 (4/93), Hayes et al., US 4,877,745 (10/89), Kimura et al., "An Immobilized Enzyme Membrane Fabrication Method Using an Ink Jet Nozzle," Biosensors 40:41-52 (1988), Kuriyama, JP Sho 63-223557 (9/88), Miyagi et al., JP 59-24244 (2/84), Madou et al., US 4,874,500 (10/89), Chang, US 4,591,570 (5/86), Chang, WO 84/03151 (8/84), Clark et al., US 4,728,591 (5/88), Cozzette et al., US 5,200,051 (4/93), Ekins, "Developments In Immunoassay Methods," Biochimica Clinica Suppl. 1/8:13 (1989), Ekins, US 5,432,099 (11/95), Ekins et al., "Fluorescence Spectroscopy and its Application to a New Generation of High Sensitivity, Multi-Microspot, Multianalyte, Immunoassay," Clinica Chimica Acta 194:91-114 (1990), Geysen, WO 84/03564 (9/84),

Gordon et al., EP 0 063 810 A1 (11/82), Herzberg and Fish, EP 0 171 150 B1 (2/86), Huang, US 4,327,073 (4/82), Humphries et al., US 4,704,353 (11/87), Johnson, US 4,216,245 (8/80), Kleinfeld et al., "Controlled Outgrowth of Dissociated Neurons on Patterned Substrates," J. Neuroscience 8:4098-4120 (1988), Lowe and Earley, US 4,562,157 (12/85), Madou et al., US 4,874,500 (10/89), Craig et al., "Ordering of Cosmid Clones Covering the Herpes Simplex Virus Type I (HSV-I)" Genome, Nuc. Acids. Res. 18:2653-2660 (1990), Gergen et al., "Filter Replicas and Permanent Collections of Recombinant DNA Plasmids," Nucleic Acids Res. 7:2115-2135 (1979), Gillespie, *et al.*, US 4,483,920, (11/84), Hanahan & Meselson, "Plasmid Screening at High Colony Density," Gene 10:63-67, (1980), Hanahan & Meselson, "Plasmid Screening at High Colony Density," Methods in Enzymology 100:333-342, (1983), Kohara *et al.*, "The Physical Map of the Whole E. coli Chromosome: Application of a New Strategy for Rapid Analysis and Sorting of a Large Genomic Library," Cell 50: 495-508 (1987), White *et al.*, US 4,677,054 (6/87), Arnold, Jr., US 5,362,866 (11/94), Damagupta et al., EP 0 281 927 A2 (9/88), Frank, *et al.*, "Simultaneous Synthesis and Biological Applications of DNA Fragments: An Efficient and Complete Methodology," Methods in Enzymology 134:221-251 (1987), Groet, *et al.*, US 4,533,682 (5/86), Guire, US 4,973,493 (11/90), Macevicz, US 5,002,867 (5/91), Southern and Maskos, WO 90/03382 (4/90), and/or Urdea et al, US 4,517,338 (5/85).

14. Claims 1-13 and 15-25 of the '305 patent are rendered obvious under 35 U.S.C. 103 in view of Chang, US 4,591,570 (5/86) in combination with Cozzette et al., US 5,200,051 (4/93), Hayes et al., US 4,877,745 (10/89), Kimura et al., "An Immobilized Enzyme Membrane Fabrication Method Using an Ink Jet Nozzle," Biosensors 40:41-52 (1988), Kuriyama, JP Sho 63-223557 (9/88), Miyagi et al., JP 59-24244 (2/84), Madou et al., US 4,874,500 (10/89), Damagupta et al., US 5,348,855 (9/94), Drmanac et al., US 5,202,231 (8/93), Eggers, *et al.*, US 5,532,128 (7/96), Erlich et al., EP 0 237 362 B1 (9/87), Khrapko et al., "An Oligonucleotide Hybridization Approach to DNA Sequencing," FEB 256:118-122 (1989), Khrapko et al., "Hybridization of DNA with Oligonucleotides Immobilized in Gel," Molecular Biology 25:581-591 (1991), Lysov et al., "A New Method For Determining the DNA Nucleotide Sequence By Hybridization With Oligonucleotides," Doklady Biochemistry 303:355-452 (1988), Palva et al., GB 2 156

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The following references show features that illustrate or suggest the combination of a multitude of features that became available at various times to persons of ordinary skill, which features limit or render the claims of the '305 patent anticipated under 35 U.S.C. §102 or obvious under 35 U.S.C. §103.

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EXHIBIT 6

COPY

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IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF CALIFORNIA
SAN FRANCISCO

AFFYMETRIX, INC.,

Plaintiff and counterdefendant,

v.

SYNTENI, INC. and INCYTE PHARMACEUTICALS, INC.,

Defendants and counterplaintiffs.

Case No. C98-4508 FMS (MEJ)

INITIAL DISCLOSURE OF PRIOR ART PURSUANT TO 16-7

In accordance with Civil L.R. 16-7, Defendants Incyte Pharmaceuticals, Inc. and Synteni, Inc., hereby submit this initial disclosure of prior art developed to date relating to U.S. Patent No. 5,800,992 ('992 Patent). Defendants are actively engaged in searching for other prior art and persons working in the technologies to which the '992 patent relates. Defendants anticipate that such effort may yield additional prior art of comparable relevance to what is disclosed below, and defendants intend to supplement this disclosure as such additional prior art is located.

Prior Art Affecting the Validity of U.S. Patent No. 5,800,992

Defendants' investigation to date has resulted in the identification of the following prior art references that appear, on their face, to anticipate or render obvious Claims 1 and 3-5 of the '992 Patent. Defendants acknowledge that numerous disputed issues of claim construction may lie ahead, altering significantly the manner in which a determination of patent validity under 35 U.S.C. §§ 102 and 103 would be carried out. Claim interpretation issues may be particularly significant in light of plaintiff's having copied portions of Claims 4 and 5 of the '992 patent from a patent application belonging to Defendants. Defendants also acknowledge that issues of enablement may affect the scope or relevance of certain prior art. Defendants have accepted the disclosed prior art at face value and have made no attempt, at this preliminary stage, to evaluate the future impact of claim construction and enablement issues that may be presented.

The asserted claims 1 and 3-5 of the '992 patent when interpreted as broadly as Affymetrix appears to be interpreting them, are invalid under 35 U.S.C. §102 as anticipated by, or under 35 U.S.C. §103 as obvious in view of, the following prior art references.

1. Claims 1 and 3-5 of the '992 patent are anticipated by USPN 5,213,882 (Bahl, issued 6/1993, filed 11/1989), or obvious in light of Bahl, in combination with Southern (WO/89/10977), Hanahan *et al.*, "Plasmid screening at high colony density", *Gene*, 10:63-67 (1980), Hanahan *et al.*, "Plasmid screening at high colony density", *Methods in Enzymology*, 100:333-342 (1983), Tkachuk *et al.*, "Detection of *bcr-abl* Fusion in Chronic Myelogenous Leukemia by in Situ Hybridization", *Science*, 250:559-562 (10/1990), Nederlof *et al.*, "Multiple Fluorescence In Situ Hybridization", *Cytometry*, 11:(1):126-31 (1990), and/or Hopman *et al.*, "Bi-color detection of two target DNAs by non-radioactive in situ hybridization.", *Histochemistry*, 85:1-4 (1986).
2. Claims 1 and 3-5 of the '992 patent are anticipated by EP0392546 (Dramanac, 10/17/1990), or obvious in light of Dramanac in combination with Bahl, Southern, Hanahan, Tkachuk, Nederlof, and/or Hopman (see above).
3. Claims 1 and 3-5 of the '992 patent are invalid as obvious under 35 U.S.C. 103 in light of USPN 4,981,783 (Augenlicht, issued 1/1991, filed 4/1986), Dramanac, Bahl, Southern, Hanahan, Tkachuk, Nederlof, Hopman and/or Fromgarts *et al.*, "[Preparation of

fluorescein-labeled DNA and its use as a probe in molecular hybridization]", *Bioorg Khim*, 12:1508-13 (1986).

4. Claims 1 and 3-5 of the '992 patent are invalid as obvious under 35 U.S.C. 103 in light of Augenlicht *et al.*, "Expression of Cloned Sequences in Biopsies of Human Colonic Tissue and in Colonic Carcinoma Cells Induced to Differentiate *In Vivo*", *Cancer Research*, 47:6017-6021 (1987), Drmanac, Bahl, Southern, Hanahan, Tkachuk, Nederlof, Hopman and/or Frumgarts.

5. Claims 1 and 3-5 of the '992 patent are invalid as obvious under 35 U.S.C. 103 in light of Saiki *et al.*, "Genetic analysis of amplified DNA with immobilized sequence-specific oligonucleotide probes", *Proc. Natl Acad. Sci. USA*, 86:6230-6234 (1989), Augenlicht, Drmanac, Bahl, Southern, Hanahan, Tkachuk, Nederlof, Hopman and/or Frumgarts.

6. Claims 1 and 3-5 of the '992 patent are invalid as obvious under 35 U.S.C. 103 in view of Scharf *et al.*, "HLA class II allelic variation and susceptibility to pemphigus vulgaris", *Proc. Natl. Acad. Sci. USA*, 85:3504-3508, (1988), USPN 5,310,893 (Erlich, issued 10/1994, filed 5/1989), EP0235726 (Damagupta, 9/1987), Augenlicht, Drmanac, Bahl, Southern, Hanahan, Tkachuk, Nederlof, Hopman and/or Frumgarts.

The following references show features that illustrate or suggest the combination of a multitude of features that became available at various times to persons of ordinary skill, which features limit or render the claims of the '992 patent anticipated under 35 U.S.C. § 102 or obvious under 35 U.S.C. § 103.

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Dated: February 26, 1999

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EXHIBIT 7

REDACTED IN ITS ENTIRETY

EXHIBIT 8

REDACTED IN ITS ENTIRETY

EXHIBIT 9

DOCKET NO: 9561/006/27SD

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF:
T.D. SHALON, ET AL. GROUP ART UNIT: 1634

SERIAL NO: 08/514,875 EXAMINER: MARSCHEL

FILED: AUGUST 14, 1995

FOR: METHOD FOR ANALYZING GENE EXPRESSION PATTERNS

DECLARATION OF KRICKA

ASSISTANT COMMISSIONER FOR PATENTS
WASHINGTON, D.C 20231

SIR:

I, Larry Kricka, do hereby declare and state that:

1. I have been retained by Incyte Pharmaceuticals, Inc., who I understand to be a licensee of the above-captioned patent application. I am a citizen of the United Kingdom and a Permanent Resident of the United States of America. I am being paid a fee of $325 per hour. My compensation is in no way dependent on the outcome of any proceeding, be it an interference or litigation, or the issuance of the above-captioned patent application. Further, I have read and am familiar with U.S. Patent 5,800,992 as well as the application originally filed as U.S. Patent Application Serial No. 08/670,118, filed June 25, 1996, which is attached hereto as Exhibit 1 to my Declaration. I further state that I have substantial experience and expertise in clinical

diagnostics, microanaltyical techniques and ligand binding assays. My Curriculum Vitae is attached hereto as Exhibit 2.

2. I have reviewed the '992 patent, and claims 4 and 5 thereof.

In order to practice whatever process is recited in Claim 4 of the '992 patent, one must be able to prepare the "array of polynucleotides representing a plurality of known genes derived from the two cell types" referred to in Claim 4. Claim 5 of the '992 patent specifies that the "array of polynucleotides is formed on a substrate with a surface having an array of at least 10^3 distinct polynucleotides in a surface area of about 1 cm^2, each distinct polynucleotide being disposed at a separate, defined position." I have reviewed Exhibit 1 hereto to determine if it contains a written disclosure that would teach one of ordinary skill in the art how to prepare such an array in a fashion that would be effective to hybridize to nucleic acids obtained from two different cell types differentially labeled, as required by Claim 4 of the '992 patent. Exhibit 1, and the '992 patent, do not contain such a teaching.

3. The level of skill in the art to which Exhibit 1 is directed is, as of 1990 and today, remarkably high. The ordinary artisan, to my understanding, holds an MD, a Ph D or similar degree, or the experiential equivalent thereof, as well as at least a limited amount of laboratory experience.

4. Exhibit 1 identifies several separate methods of making the necessary array. First, the '992 patent teaches attaching each necessary reagent to a separate specific position on a solid matrix. Col. 19, lines 48 - 54. This method refers, however, only to the attachment of oligonucleotides of at most ten nucleotides in length (10-mers), and is not taught or shown to be useful in connection with polynucleotides. The second method referred to is identified as a

"caged biotin type linking". No reference is given for this technology, and the patent teaches that it to is confined to the preparation of oligonucleotides of 10 nucleotides (or presumably less) Elsewhere, U.S. Patent 5,252,743 is referred to in connection with this technology. This patent does not refer to polynucleotides at all. U.S. Patent 5,143,854 is also identified as providing methods for synthesizing oligonucleotides of this size at Column 19, lines 59 - 65 of the '992 patent. Methods that provide, at maximum, oligonucleotides on the substrate surface of 10 nucleotides or less would not appear to satisfy the requirement of Claim 4, nor would they be sufficient to result in hybridization of all nucleic acids obtained from any given cell, which appears to be a requirement of Claim 4 of the '992 patent. Accordingly, these methods, taught as useful in the preparation of arrays of oligonucleotides, would not be used by the reader to prepare the array of polynucleotides required by Claims 4 and 5. The claims are specifically directed towards use of an "array of polynucleotides" but nowhere does the specification of the '992 patent define what a polynucleotide is. Most of the discussion in the '992 patent of synthesizing nucleotide sequences is by photolithography, on a matrix having positionally defined regions, and is directed and confined to synthesis of oligonucleotides. In the context of the '992 patent, an oligonucleotide and a polynucleotide must be different entities, as evidenced by the use of these terms (see col 4, lines 30-36; col 4, lines 10-11 and lines 35-38; col 6, lines 49-51; col 12 lines 52-55; col 18, lines 17-20).

5. The '992 patent describes 10-mer sequences as oligonucleotides, polynucleotides would at least be larger than this. Further, the '992 patent refers to oligonucleotide probes of "greater than about 25 nucleotides" (col 28, lines 36-37)as well as longer lengths ("greater than e.g. about fifty nucleotides") (col 28, lines 41-42). The method

described for synthesis of these oligonucleotides is a system of photolithography This method is described at various portions of the specification of the '992 patent, and exemplified at Column 62, line 35 - Column 71, line 21. This method is exemplified as giving dimers and trimers, not the polynucleotides required by Claim 4, and is described at column 68, lines 58-67; column 69, lines 1- 10 as providing 10-mers The only reference to the formation of polynucleotides larger than this (in terms of the number of nucleotides comprising the polynucleotide) is the language at column 68, lines 28 -31, which asserts the possibility of forming dodecanucleotides and "larger polynucleotides." Methods to form these polynucleotides are not exemplified or further described. For reasons discussed below, one of skill in the art as of 1990 - 1996 could not prepare an array of polynucleotides required by Claim 4 of the '992 patent on the basis of the synthetic method described.

6. Technology of this type requires a repetitive photoprotection, photodeprotection and synthesis method for each nucleotide added to the probe to be synthesized. This method is addressed in U.S. Patent 5,744,305, issued to Affymetrix, and naming as a co-inventor Michael Pirrung, who is also the lead inventor of U.S. Patent 5,143,854 incorporated by reference in the '992 patent for its teaching of a synthesis method applicable to oligonucleotide-based arrays, column 19, lines 59 -65 of the '992 patent. Pirrung with others has recently indicated that this technology, without more, will not allow the preparation of arrays of DNA of sufficient purity and fidelity as to perform the method of Claim 4 or 5 of the '992 patent. Recent papers published in the Journal of Organic Chemistry (1995, 60, 6270-6276 and 1998, 63, 241-246) by Pirrung et al indicates that there are problems in the preparation of arrays to such an extent that they motivated further experimental work:

> "It likewise requires that each deprotection and coupling reaction in each cycle proceed in as close as possible to quantitative yield in order to produce sequences of high fidelity with no deletions, since no intermediate purification steps can be performed. Because light-directed synthesis of different sequence is simultaneously conducted at many locations on the same surface, it also has the unique trait that the incorporation of "extra" monomer units can result form light falling in unintended regions. This latter limitation to the production of high-quality arrays of DNA can be addressed both through the physics of the masking process and through novel photochemistry. The former limitation can be addressed by optimizing the chemistry of both the deprotection and coupling steps; that topic provided the motivation for this work."
> (Journal of Organic Chemistry, 1995, 60, page 6271).

Pirrung also points out a pertinent facet of the previous array work, namely that:

> "no direct measures of the fidelity of the DNA synthesized in this work were reported" in the work described by Pease et al in PNAS 1994,91.5022-6. (page 6271).

He also indicates that there are still unsolved problems in array fabrication as of 1995 and that these are related specifically to the photochemical synthesis method:

> "These experiments are encouraging in that DNA can be effectively prepared with photochemical deprotection steps, but they suggest that a problem unique to photochemical DNA synthesis must be solved in order to prepare the highest-quality DNA arrays using light-directed synthesis" (page 6271)

and that in syntheses of CTTT and CTT oligomers that the yields using the photoprotection agent MeNPOC were considerably less than the control synthesis using a DMT group.

> "MeNPOC-based synthesis ..... did give an average step yield of 92.7% for the preparation of the target sequence based on DMTr release, and the quantitative HPLC yield was 60% of the control." (page 6276)

> "The MeNPOC-based synthesis gave an average step yield of 89.1% based on the DMTr release and a quantitative HPLC yield of 77.6% of the control." (page 6276)

He concludes that:

> "This study has demonstrated that photochemical deprotection steps in solid-phase DNA synthesis can result in

oligonucleotides of diminished quality." (page 6276).

He specifically points out a problem derived from the inappropriate choice of a protecting group:

> "The photochemical degradation of benzoylcytidine was identified as one problem, but it could be solved by changing protecting groups." (page 6276)

He expresses a concern about the quality of arrays:

> "These data raise concern about the quality of the DNA that has been prepared in array synthesis experiments." (page 6276).

and about the synthesis yields:

> "If the yield for two couplings observed here (approx 66%) is representative of similar reactions on a flat surface, the amount of the intended DNA sequences within each synthesis area in the experiments reported by Pease et al (involving four photochemical couplings) would be <50%. When this yield is extrapolated to the octanucleotides necessary for reasonable DNA reading length in SBH, the amount of desired sequences

would be <20%, and this value reflects only errors that can be ascribed to chemistry " (page 6276).

and finally comments on the effect of the low yields:

"This dilution of intended DNA by "junk" DNA will obviously raise the signal-to-noise ratio in subsequent hybridization experiments." (page 6276).

7. The '992 patent specification warns against the photoreactivity of side chain protecting groups (col 67, lines 6-9; col 40, lines 9-17) and cites standard protecting groups for adenine, cytosine and guanine and states "other amides of the general formula I-COR (R=ALKYL, ARYL) where R may be alkyl, aryl have been used." (Col 39 and 40). However, the literature on photodeprotection shows that cytidine protected with a benzoyl group is photo-unstable and leads to low yields of coupled product (MC Pirrung and J-C Bradley, Journal of Organic Chemistry 1995, 60, 6270-6278 reiterated in their article in Journal of Organic Chemistry 1998, 63, 241-246).

All statements made herein of my own knowledge are true, and all statements made on information and belief are believed true. I am aware that willful false statements and the like are punishable by fine, imprisonment or both. 18 U.S.C. §1001, and that such willful false statements may jeopardize the validity of the above-captioned patent application and any patent to issue thereon.

DATE: October 26, 1998

Larry J. Kricka

LARRY KRICKA

EXHIBIT 10

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Paper No. 60

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

PATRICK O. BROWN and TIDHAR D. SHALON
(08/514,875),

Junior Party,

v.

STEPHEN P.A. FODOR, DENNIS W. SOLAS,
and WILLIAM J. DOWER
(5,800,992),

Senior Party.

Interference No. 104,358

HEARD: 9 AUGUST 1999

Before WILLIAM F. SMITH, SCHAFER, and TORCZON, Administrative Patent Judges.

TORCZON, Administrative Patent Judge.

DECISION

(UNDER 37 CFR § 1.617)

This matter was heard pursuant to an Order to Show Cause (Paper No. 3 (Ord. Show Cause, 7 April 1999)). Junior party Brown has not met its burden of establishing *prima facie* that it is entitled to judgment relative to senior party Fodor.

35 U.S.C. § 135(c) Notice: Failure to file a copy of any agreement regarding the termination of this proceeding may render the agreement and any resulting [illegible]. See section 135(c) and 37 CFR § 1.661 for more details.

Background

During prosecution of its 08/514,875 ("'875") application, Brown requested an interference with Fodor's 5,800,992 ("'992") patent[1] (Brown '875 Paper No. 28 (Req. Decl'n Interf.) at 1). In its request, Brown gives the following reasons why it is *prima facie* entitled to judgement relative to Fodor: (1) Fodor '992 fails to comply with the written description requirement of 35 U.S.C. § 112[1] and (2) Fodor '992 fails to comply with the enablement requirement of 35 U.S.C. § 112[1] (Brown '875 Paper No. 28 at 4).

To establish a *prima facie* case entitling a junior party to proceed with the interference, the junior party must prove at least so much of its case as would entitle it to an award of priority if the senior party were to rely only on its filing date and were not to rebut any of the junior party's case. Hahn v. Wong, 892 F.2d 1028, 1032, 13 USPQ2d 1313, 1317 (Fed. Cir. 1989), citing Kistler v. Weber, 412 F.2d 280, 285, 162 USPQ 214, 218 (CCPA 1969). In the present case, Brown does not attempt to prove that it has a priority date earlier than the 6 December 1990 filing date accorded to Fodor (Interf. 104,358 ("'358"), Paper No. 1 (Not. Decl'g Interf.) at 41). Rather, Brown argues that Fodor is not entitled to the filing date it was accorded because the Fodor '992 disclosure did not adequately describe or enable the claimed, interfering subject matter.

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[1] Which issued from application 08/670,118.

The claims of Fodor corresponding to the count of the interference are reproduced below (Fodor '992 at 82:53-84:3):

> 4. A method of detecting differential expression of each of a plurality of genes in a first cell type with respect to expression of the same genes in a second cell type, said method comprising:
> adding a mixture of labeled nucleic acid from the two cell types to an array of polynucleotides representing a plurality of known genes derived from the two cell types, under conditions that result in hybridization to complementary-sequence polynucleotides in the array; and
> examining the array by fluorescence under fluorescence excitation conditions in which polynucleotides in the array that are hybridized to labeled nucleic acid derived from one of the cell types give a distinct fluorescence emission color and polynucleotides in the array that are hybridized to labeled nucleic acid derived from the other cell types give a different fluorescence emission color.
>
> 5. The method of claim 4, wherein the array of polynucleotides is formed on a substrate with a surface having an array of a least 10^3 distinct polynucleotide [sic] in a surface area of about 1 cm^2, each distinct polynucleotide being disposed at a separate, defined position in said array.

35 U.S.C. § 112[1] - written description

To fulfill the written description requirement, the specification must clearly convey to a person having ordinary skill in the art that the inventor had possession of the invention claimed. Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). The subject matter of a claimed invention need not be described identically or literally for an application to satisfy the written description

requirement. Kennecott Corp. v. Kyocera Int'l Inc., 835 F.2d 1516, 1520, 222 USPQ 369, 372 (Fed. Cir. 1984).

Ward, a Brown declarant, states that the Fodor disclosure does not describe the claim 4 method of adding a mixture of labeled nucleic acid from two different cell types to an array where the nucleic acid from each cell type is labeled with a differently colored fluorescent label for the purpose of detecting differential expression of a gene in one cell type with respect to expression of that same gene in a second cell type. Specifically Ward argues that Fodor does not teach simultaneous detection of the same gene using the claimed labeling method but rather simultaneous detection of different genes using this method. (Brown '875 Paper No. 28., Att. (Ward Decl'n) at 3-5).

Ward cites the following portion of the Fodor disclosure in support of its conclusion (Fodor '992 at 52:3-9):

> In another embodiment, different targets may be simultaneously sequenced where each target has a different label. For instance, one target could have a green fluorescent label and a second target could have a red fluorescent label. The scanning step will distinguish sites of binding of the red label from those binding the green fluorescent label. Each sequence can be analyzed independently from one another.

While Ward acknowledges that this portion of the disclosure describes how one can sequence two different targets (e.g., nucleic acids) simultaneously using different labels, Ward argues that the Fodor claims in question require simultaneous analysis of the same target from two different cell types and that such

analysis is not described in the cited portion of the Fodor disclosure or elsewhere in the Fodor disclosure (Brown '875 Paper No. 28, Att. (Ward Decl'n) at 4-5).

Fodor discloses simultaneous analysis of the same nucleic acids from different cells types within the disclosure. For instance, Fodor teaches methods of characterizing and distinguishing cells based on their stage of development (Fodor '992 at 35:12-30). Two separate cells from a particular sample, each in a distinct stage of development are different cell types since the cells are structurally different (Fodor '992 at 30:10-20).

In Fodor's method, one way of distinguishing cells according to their stage of development is by determining whether a particular messenger RNA (mRNA) is present or expressed in each cell, using fingerprinting or mapping techniques. Therefore, Fodor teaches probing different cell types for the same mRNA. This determination of whether mRNA is present or not is used to distinguish closely related cell types.

In further describing this method, Fodor notes that "[m]eans to simultaneously screen a plurality or very large number of different sequences are provided", but does not identify such means at this portion of the disclosure (Fodor '992 at 35:12-30). In the portion of the disclosure Ward cites, Fodor teaches labeling targets (e.g., nucleic acids) with distinctly colored fluorescent labels as one means of simultaneously

sequencing targets (Fodor '992 at 52:3-9). Fodor teaches sequencing as encompassing fingerprinting and mapping (Fodor '992 at 7:6-18 and 9:35 to 10:12) and teaches that the same labeling means are used for all three techniques (Fodor '992 at 28:1-5 and 32:55-58). One looking within the Fodor disclosure for a means of simultaneously characterizing and distinguishing mRNA from more than one cell type using fingerprinting or mapping techniques would be led to the disclosed technique of labeling targets (e.g., mRNA) with distinctly colored fluorescent labels.

Brown has not presented a preponderance of the evidence that the Fodor specification would not have clearly conveyed to a person having ordinary skill in the art that the Fodor inventors had possession of the invention as claimed.

35 U.S.C. § 112[1] - enablement

Any analysis of whether a particular claim is supported by the disclosure in an application requires a determination of whether that disclosure, when filed, contained sufficient information regarding the subject matter of the claims to enable one skilled in the pertinent art to make and use the claimed invention. In re Wands, 858 F.2d at 731, 735, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). A specification that contains a teaching of the manner and process of making and using an invention in terms that correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of

35 U.S.C. § 112[1] unless there is a reason to doubt the objective truth of the statements that must be relied on for enabling support. In re Cortright, 165 F.3d. 1353, 1357, 49 USPQ2d 1464, 1466 (Fed. Cir. 1999).

Brown argues that Fodor's claim 4 method of "detecting differential expression" was not enabled for the step of comparing the gene expression detected within the two different cell types such that a ratio analysis can be performed (Brown '875 Paper No. 28, Att. (Ward Decl'n) at 13).

As noted above, Fodor describes methods for distinguishing closely related cell types based on whether or not a particular mRNA is present or expressed (Fodor '992 at 35:21-26). In order to distinguish two things, one must necessarily compare those things to note similarities and differences. We find that a step of comparing is inherent in a method of distinguishing.

Relying on the Ward declaration for support (Brown '875 Paper No. 28, Att. (Ward Decl'n) at 7-8), Brown argues that since it is so difficult to label mRNA in a way that will result in a strong, detectable signal, one skilled in the art would be unable to practice the claimed invention. Ward acknowledges that, as of 1990, reagents for direct labeling of RNA were known but argues that labeling would be difficult to practice with all possible differential expression that might be performed using the method of Fodor's claim 4 (Brown '875 Paper No. 28 at 14-15).

The enablement requirement is met if the description enables any mode of making and using the claimed invention. Engel Indus., Inc. v. Lockformer Co., 946 F.2d 1528, 1533, 20 USPQ2d 1300, 1304 (Fed. Cir. 1991). Ward notes it was possible to label RNA directly at the time of the invention. Even if some embodiments within the scope of the claims would be difficult or even impossible to complete, the claimed invention may still be enabled. Disclosure in the specification sufficient to enable one skilled in the art to practice the invention is all that 35 U.S.C. 112[1] requires for enablement. It is not a function of the claims to exclude all possible inoperative embodiments. Atlas Powder Co. v. E.I. duPont de Nemours & Co., 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984).

Moreover, Fodor's claim 4 does not require that all genes of a cell type be detected, only a "plurality" of genes (Fodor '992 at 82:53-56). The fact that a portion of a cell's mRNA sequences may be difficult or impossible to label effectively does not prevent one from practicing Fodor's invention because expression of each of the cell's remaining genes may still be detected.

Relying on the Kricka declaration for support, Brown argues that the disclosure of Fodor does not teach one skilled in the art how to make polynucleotide probes of all lengths for the array, which Brown urges would be necessary to make Fodor's claim 4 useful (Brown '875 Paper No. 28 at 15). Kricka acknowledges that Fodor describes an oligonucleotide comprising

ten nucleotides but argues that oligonucleotides of this limited length would not be sufficient to result in hybridization of all nucleic acids obtained from a given cell as Fodor's claims 4 and 5 require (Brown '875 Paper No. 28, Att. (Kricka Decl'n) at 2-3).

Kricka's interpretation of claims 4 and 5 is not correct. Neither claim requires that all the nucleic acids obtained from a given cell be labeled and detected. The claims require analysis of the expression of a "plurality of genes" from a cell type via addition of a mixture of "labeled nucleic acid" to an array. Probes of length ten would be sufficient to hybridize to at least some of the nucleic acids of a cell.

Kricka further states that the formation of polynucleotides having lengths greater than ten nucleotides and having sufficient purity and fidelity to perform the methods of Fodor's claims 4 and 5 would not be possible. Kricka relies primarily on statements appearing in a 1995 article authored in written in part by Pirrung[2] (Brown '875 Paper No. 28, Att. (Kricka Decl'n) at 4-8).

Kricka's reliance on the Pirrung article is misplaced. The synthesis method described in the article uses glass *beads* as a substrate (Pirrung at 6271), not glass *slides* as Fodor discloses in one embodiment (Fodor '992 at 63:27). Brown provides no nexus

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[2] Michael C. Pirrung & Jean-Claude Bradley, Comparison of Method for Photochemical Phosphoramidite-Based DNA Synthesis, 60 J. Org. Chem. 6270-6276 (1995) (Pirrung).

between the problems noted in the Pirrung article and the different method Fodor disclosed.

Even assuming the Pirrung article describes an analogous synthesis method, Pirrung does not support a conclusion that the Fodor disclosure lacks enablement. The Pirrung article highlights the difficulties one encounters when undertaking light-directed, solid-phase DNA synthesis. For instance the authors state that "[light-directed synthesis] likewise requires that each deprotection and coupling reaction in each cycle proceed in as close as possible to quantitative yield in order to produce sequences of high fidelity with no deletions, since no intermediate purification step can be performed" (Pirrung at 6271) and that "...photochemical deprotection steps in solid-phase light directed DNA synthesis can result in oligonucleotides of diminished quality" (Pirrung at 6276). Perfection or optimization of an invention, however, is not a requirement of enablement. Atlas Powder Co., 750 F.2d at 1577, 224 USPQ at 414. Nowhere does the Pirrung article state that the light-directed method of synthesis will not work. In fact, Pirrung states that light-directed synthesis is advantageous in preparing large, high-density arrays of polymer sequences to enable sequencing-by-hybridization (citing Pat. No. 5,143,854, which is incorporated by reference into the Fodor '992 disclosure (Fodor '992 at 20:2-4)).

Brown has failed to establish a threshold case by a preponderance of the evidence that Fodor's disclosure would not have enabled one skilled in the pertinent art to make and use the claimed invention.

Conclusion

Brown has not met its burden of establishing that it is *prima facie* entitled to judgement relative to Fodor by a preponderance of the evidence.

ORDER

Upon consideration of the record of this interference, it is ORDERED that judgment on priority as to the count is awarded against junior party Brown.

WILLIAM F. SMITH
Administrative Patent Judge

RICHARD E. SCHAFER
Administrative Patent Judge

RICHARD TORCZON
Administrative Patent Judge

BOARD OF PATENT
APPEALS
AND
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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

PATRICK O. BROWN and TIDHAR D. SHALON
(08/688,488),

Junior Party,

v.

STEPHEN P.A. FODOR, LUBERT STRYER,
J. LEIGHTON READ, and MICHAEL C. PIRRUNG
(5,744,305),

Senior Party.

Interference No. 104,359

HEARD: 9 AUGUST 1999

Before WILLIAM F. SMITH, SCHAFER, and TORCZON, Administrative Patent Judges.

TORCZON, Administrative Patent Judge.

DECISION

(UNDER 37 CFR § 1.617)

This matter comes to us pursuant to an Order to Show Cause issued by Administrative Patent Judge McKelvey (Paper No. 3 (Ord. Show Cause, 7 April 1999)). Junior party Brown has not met its burden of establishing *prima facie* that it is entitled to a judgment relative to senior party Fodor.

35 U.S.C. § 135(c) Notice: Failure to file a copy of any agreement regarding the termination of this proceeding may render the agreement and any resulting patents unenforceable. See section 135(c) and 37 CFR § 1.661 for more details.

Background

During the prosecution of its 08/688,488 ("'488") application, Brown requested an interference with Fodor's 5,744,305 ("'305") patent[1] (Brown '488 Paper No. 30 (Req. Decl'n Interf.) at 1). In that request, Brown gives the following reasons why it is *prima facie* entitled to judgement relative to Fodor: (1) Fodor '305 fails to comply with the written description requirement of 35 U.S.C. § 112[1] and (2) Fodor '305 fails to comply with the enablement requirement of 35 U.S.C. § 112[1] (Brown '488 Paper No. 30 at 4).

To establish a *prima facie* case entitling a junior party to proceed with the interference, the junior party must prove at least so much of its case as would entitle it to an award of priority if the senior party were to rely only on its filing date and were not to rebut any of the junior party's case. Hahn v. Wong, 892 F.2d 1028, 1032, 13 USPQ2d 1313, 1317 (Fed. Cir. 1989), citing Kistler v. Weber, 412 F.2d 280, 285, 162 USPQ 214, 218 (CCPA 1969). In the present interference, Brown does not attempt to prove that it has a priority date earlier than the 6 June 1995 filing date accorded to Fodor (Interf. 104,359 ("'359") Paper No. 1 (Not. Decl'g Interf.) at 41). Rather, Brown argues that Fodor is not entitled to the filing date it was accorded because the original Fodor '305 disclosure did not

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[1] Which issued from application 08/466,632 ("'632").

adequately describe or enable the claimed, interfering subject matter.

Fodor's claim 1 defines the following subject matter (Fodor '305 at 41:10-20):

> 1. An array of oligonucleotides, the array comprising:
> a planar, non-porous solid support having at least a first surface; and
> a plurality of different oligonucleotides attached to the first surface of the solid support at a density exceeding 400 different oligonucleotides/cm^2, wherein each of the different oligonucleotides is attached to the surface of the solid support in a different predefined region, has a different determinable sequence, and is at least 4 nucleotides in length.

35 U.S.C. § 112[1] - written description

To fulfill the written description requirement, the specification must clearly convey to a person having ordinary skill in the art that the inventor had possession of the invention claimed. Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). Brown contests the adequacy of Fodor's description on four specific grounds: non-porosity, polynucleotides, surface density, and sequence length.

1. Non-porosity

Brown acknowledges that Fodor discloses a glass slide as a substrate useful in the invention, but argues that "[t]he identification of a glass slide, per se, is insufficient to support the limitation to non-porous" (Brown '488 Paper No. 30 at 13). Kricka, Brown's declarant, does not dispute the fact that a glass slide is non-porous. Rather, Kricka argues that the Fodor specification does not reasonably convey to one skilled in

the art that the Fodor applicants had recognized a non-porous substrate as an important element of their invention (Brown '488 Paper No. 30, Att. (Kricka Decl'n) at 5).

The subject matter of a claimed invention need not be described identically or literally for an application to satisfy the written description requirement. By disclosing a device (i.e., a glass slide) that inherently performs a function or has a property (i.e., non-porosity), a patent applicant necessarily discloses that function or property even though he says nothing concerning it. Kennecott Corp. v. Kyocera Int'l Inc., 835 F.2d 1516, 1520, 222 USPQ 369, 372 (Fed. Cir. 1984). While Fodor does not use the term "non-porous" in hæc verba, Brown has not established that a preponderance of the evidence shows a lack of written description for this limitation.

Brown argues that the Gait reference[2], which Fodor '305 incorporates by reference (Fodor '305 at 27:48-51) teaches a preference for porous glass as a substrate. While the Gait reference teaches that supports used in solid-phase synthesis should be macroporous (Gait at 45), the discussion in Gait is limited to the use of silica or porous glass *beads* as a substrate for oligonucleotide synthesis. Gait does not discuss synthesis of these oligonucleotides on glass *slides*. Since Gait concerns only silica or glass beads, the reference provides no evidence

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[2] Michael J. Gait, Oligonucleotide Synthesis: A Practical Approach (1984). (Gait).

concerning the propriety of the use of the limitation "non-porous" as it relates to Fodor's disclosure of glass slides[3].

2. Polynucleotides

We noted at the outset that "polynucleotides" only appears in claims 15-26 of the Fodor patent. Even if Brown were successful with this line of argument, Fodor could still rely on claims 1-14 for priority since these claims also correspond to the count.

Brown argues that the Fodor disclosure contains no specific support for the term "polynucleotides" as it appears in claim 15 of the Fodor patent (i.e., as a probe attached to the substrate of the array) (Brown '488 Paper No. 30 at 14). Claim 15 defines the following subject matter (Fodor '305 at 42:10-20):

> 15. An array of polynucleotides, the array comprising:
> a planar non-porous solid support having at least a first surface; and
> a plurality of different polynucleotides attached to the first surface of the solid support at a density exceeding 400 different polynucleotides/cm^2, wherein each of the different polynucleotides is attached to the surface of the solid support in a different predefined region, has a different determinable sequence, and is at least 4 nucleotides in length.

Fodor's invention includes the synthesis of polymer sequences on substrates (Fodor '305 at 1:47-52). Fodor discloses "the set of nucleotides" as monomers that can be joined together to form a polymer within the scope of the invention (Fodor '305

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[3] Fodor teaches the use of glass beads as an alternative to the use of glass slides (Fodor '305 at 6:38-40).

at 4:49-54). While the term "polynucleotides" is only used in describing possible receptors for the probes of the array, one skilled in the art would have recognized that polymers of "the set of nucleotides" as described would be "polynucleotides." Accordingly, Brown has not established that a preponderance of the evidence shows a lack of written description for this limitation.

3. The density limitation

Brown argues that the original disclosure of Fodor does not provide a description of the limitation in the claims where the support has a density exceeding 400 different oligonucleotides (Fodor '305 patent at claim 1) or polynucleotides (Fodor '305 patent at claim 15) per centimeter-squared ("cm^2"). Brown acknowledges that Fodor '305 contains numbers that can give a value of 400 regions per cm^2. However, this portion of the disclosure was added by amendment (Fodor '632[4] Paper No. 15, (Amdt. filed 23 Sep. 1996) at 2). Brown argues that this amendment was improper because Fodor added material to the disclosure from its prior 07/492,462 application that was not clearly incorporated by reference (Brown '488 Paper No. 30 at 15-16) into the Fodor '632 application.

To properly incorporate a document into a given disclosure, the disclosure must refer to the document in such a manner that it is apparent that the cited document is part of the referencing

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[4] Fodor '632 is the application file for Fodor '305.

disclosure. In re Lund, 376 F.2d 982, 989, 153 USPQ 625, 631 (CCPA 1967). The incorporation statement for Fodor '632 was amended when the application was filed (Fodor '632 Paper No. 5 (Prel. Amdt. "B") at 1) to state:

> This application is a Rule 60 Division of USSN 08/390,272, filed February 16, 1995, which is a File Wrapper Continuation of USSN 07/624,120, filed December 6, 1990, now abandoned, which is a continuation-in-part of USSN 07/492,462, filed March 7, 1990, now U.S. Patent No. 5,143,854, which is a continuation-in-part of USSN 07/362,901, filed June 7, 1989, now abandoned, assigned to the assignee of the present application, and incorporated herein by reference for all purposes.

Fodor's incorporation sentence is grammatically awkward. One interpretation of this sentence is that the application incorporates itself by reference: a nonsensical result. A more sensible interpretation of the sentence is that the application incorporates either one or all of the applications listed. Since there would be no apparent reason to select one application for incorporation over the other, the most sensible interpretation is that all of the applications are incorporated. Hence, the most reasonable interpretation of the sentence in question in the '632 application supports incorporation of the 07/492,462 application. The parallelism between "filed", "assigned" and "incorporated" further supports the finding that the '462 application is at least one of the subjects of the incorporation clause.

Despite the grammatical awkwardness of the sentence, it is apparent that its purpose is to incorporate subject matter from other applications. Accordingly, Brown has not established that

a preponderance of the evidence shows Fodor did not intend to include the '462 application so that Fodor '305 lacks written description of the claimed density limitation.

4. At least four nucleotides

Brown concedes that the Fodor '305 patent discloses polymers comprising four or more monomers, e.g., pentapeptides, but argues that there is no specific description for oligonucleotides or polynucleotides containing four or more nucleotides (Brown '488 Paper No. 30 at 16-17).

When interpreting a claim, words of the claim are generally given their customary meaning, unless it appears from the specification or the file history that the inventor used them differently. In re Paulsen, 30 F.3d 1475, 1480, 31 USPQ2d 1671, 1674 (Fed. Cir. 1994). Since the Fodor disclosure does not indicate that the terms "oligonucleotides" or "polymers" are to be given any extraordinary meaning, we give the terms their customary meaning.

Brown relies on an encyclopedia[5] to show that an oligonucleotide is customarily understood to contain two to fifty covalently linked nucleotides (Interf. '359 Paper No. 38 (Suppl. Reply) at 6). Consistent with this general understanding of the term, the Fodor '305 disclosure contains an example of the

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[5] McGraw-Hill Encyclopedia of Science & Technology 12:349-350 (6th. ed 1987).

synthesis of an oligonucleotide containing two nucleotides (Fodor '305 patent at 32:7-33).

We note that polymers are customarily understood to comprise repeating monomers[6]. Consistent with this general understanding of the term "polymer", the Fodor '305 disclosure contains examples of the synthesis of polymers comprising two or more and specifically four or more monomers (Fodor '305 patent at 14:19-20 and 16:31-52). As noted above, we find that the polymers described by the Fodor '305 patent include polynucleotides. Accordingly, based on the ordinary and customary meanings attributed to the terms oligonucleotide and polymer and the specific examples of the Fodor '305 disclosure, Brown has not established that a preponderance of the evidence shows one having skill in the art would not recognize that Fodor had possession of oligonucleotides, and even polynucleotides, of at least four nucleotides in length.

35 U.S.C. § 112[1] - enablement

Any analysis of whether a particular claim is supported by the disclosure in an application requires a determination of whether that disclosure, when filed, contained sufficient information regarding the subject matter of the claims to enable one skilled in the pertinent art to make and use the claimed invention. In re Wands, 858 F.2d at 731, 735, 8 USPQ2d 1400,

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[6] See, e.g. Grant & Hackh's Chemical Dictionary 462 (Roger Grant & Claire Grant, eds., 5th ed. 1987) (copy attached).

1404 (Fed. Cir. 1988). A disclosure that contains a teaching of the manner and process of making and using an invention in terms that correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. § 112[1] unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. In re Cortright, 165 F.3d. 1353, 1357, 49 USPQ2d 1464, 1466 (Fed. Cir. 1999).

Brown relies on the Kricka declaration to argue that the disclosure of Fodor would not have taught one skilled in the art how to make polynucleotides of sufficient purity and fidelity for the asserted utility (Brown '488 Paper No. 30 at 18-19). Kricka relies primarily on statements appearing in a 1995 article co-authored by Fodor co-inventor Pirrung[7].

Kricka's reliance on the Pirrung article is misplaced. The synthesis method described in the article uses glass *beads* as a substrate (Pirrung at 6271), not glass slides as disclosed by Fodor. Brown provides no evidence that the problems noted in the Pirrung article would be encountered using the different method disclosed by Fodor.

Even assuming that the Pirrung article describes an analogous synthesis method, Pirrung does not support a conclusion

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[7] Michael C. Pirrung & Jean-Claude Bradley, Comparison of Method for Photochemical Phosphoramidite-Based DNA Synthesis, 60 J. Org. Chem. 6270-6276 (1995). (Pirrung).

that the Fodor disclosure lacks enablement. Pirrung highlights the difficulties one encounters when undertaking light-directed, solid-phase DNA synthesis. For instance the authors state that "[light-directed synthesis] likewise requires that each deprotection and coupling reaction in each cycle proceed in as close as possible to quantitative yield in order to produce sequences of high fidelity with no deletions, since no intermediate purification step can be performed" (Pirrung at 6271) and that "...photochemical deprotection steps in solid-phase light directed DNA synthesis can result in oligonucleotides of diminished quality" (Pirrung at 6276). Perfection or optimization of an invention, however, is not a requirement of enablement. Atlas Powder Co. v. E.I. duPont de Nemours & Co., 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984). Nowhere does Pirrung state that the light-directed method of synthesis will not work. In fact, Pirrung states that light-directed synthesis is advantageous for preparing large, high-density arrays of polymer sequences to enable sequencing-by-hybridization (Pirrung at 6270 citing Pat. No. 5,143,854 (which issued from application 07/492,462, which is a parent application of the Fodor '632 application, and which is incorporated by reference into the '632 Fodor disclosure)).

Brown has not established by a preponderance of the evidence that Fodor's disclosure would not have enabled one skilled in the pertinent art to make and use the claimed invention.

Conclusion

Brown has not met its burden of establishing that it is *prima facie* entitled to judgement relative to Fodor by a preponderance of the evidence.

ORDER

Upon consideration of the record of this interference, it is ORDERED that judgment on priority as to the Count is awarded against junior party Brown.

WILLIAM F. SMITH
Administrative Patent Judge

RICHARD E. SCHAFER
Administrative Patent Judge

RICHARD TORCZON
Administrative Patent Judge

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GRANT & HACKH'S

CHEMICAL DICTIONARY

[American, International, European and British Usage]

Containing the Words Generally Used in Chemistry, and Many of the Terms Used in the Related Sciences of Physics, Medicine, Engineering, Biology, Pharmacy, Astrophysics, Agriculture, Mineralogy, etc.

Based on Recent Scientific Literature

FIFTH EDITION
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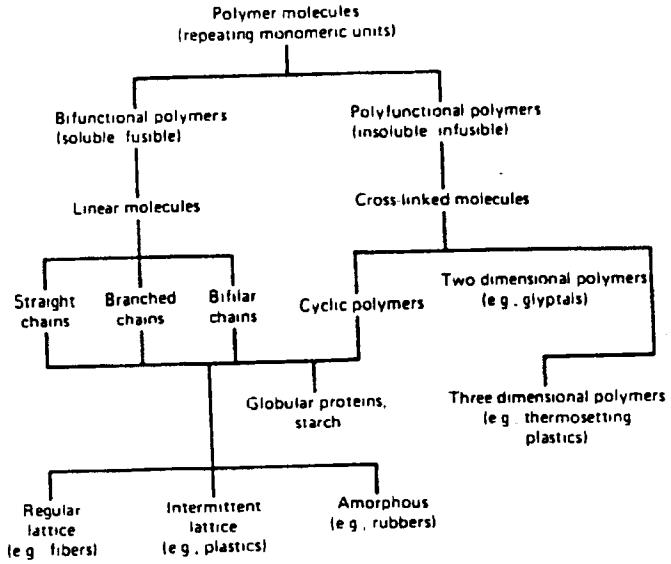

Fig 18 Classification of polymer molecules

polyhydric Polyol. A compound containing more than 2 hydroxyl groups

polyhydrone $(H_2O)_n$. A polymer of *hydrone*, q v

polyisobutylene* PIB* Poly(1,1-dimethylethylene) The polymer $(-CMe_2\cdot CH_2-)_n$

polymer Polymere, polymeride (obsolete). A member of a series of polymeric compounds A substance composed of very large molecules consisting essentially of recurring long-chain structural units that distinguish polymers from other types of organic molecules, and confer on them tensile strength, deformability, elasticity, and hardness Monomers, largely derived from coal and oil, are used to build up such polymers Considerable modification of properties results on introducing a second type of monomer (B) into the main structure (monomer A), producing a *copolymer* in which the units A and B are arranged completely at random. Alternatively, the A and B units may be arranged in order of long segments e.g., ~A−A−A−A−A−B−B−B−B−B−B−A−A−A−A−A~(*block* p). There are also *branched* polymers, in which the B units branch from the A units, and *cross-linked* polymers, in which 2 A chains are joined by one or a block of B units Polymeric molecules are classified above in Fig 18 (after Pinner). Examples of *high* polymers are plastics fibers, elastomers, human tissue Cf *macromolecular chemistry*

alloy ~ A p produced by the simultaneous polymerization of 2 substances. Cf *silicone alloy*. **blocked ~** See above **branched-chain ~** See above **co~** A composite p prepared by the polymerization of a mixture of 2 or more monomers, or of a monomer and p of low molecular weight. Cf alloy *polymer* **block ~** A p built of linearly linked polymeric units. **random ~** A p having 2 or more types of units combined in random succession in a linear-chain structure **cross-linked ~** See above. **electron-exchange ~** Redox p A polymeric structure having several sites capable of accepting or donating electrons Thus, modified cellulose with redox properties is used as a catalyst to remove oxygen from water to obtain anaerobic conditions.

graft ~ A p produced by grafting a monomer onto a straight chain p. to produce a branched-chain p. Thus, a fluorocarbon p. is heated sufficiently to form free radicals on its surface and then dipped into a monomer, e.g., styrene to produce a graft p. having a printable surface. **high ~** A p of high molecular weight, e g., containing a large number of structural units **high-trans ~** A rubbery p in which a large proportion of the C atoms are arranged in a definite pattern that repeats itself consistently in the chain, as, natural rubber **homo ~** See *tactic polymer* below. **inorganic ~** Inorganic p structures formed on heating or by catalytic action as mica, silicones inorganic rubber. **irregular ~** A p with more than one type of repeating unit **isotactic ~** A crystalline p made from 1-alkenes, in which the substituents in the asymmetric C atoms all have the same configuration relative to the main chain **linear ~** A p. in which the molecules are essentially in the form of long chains **organized ~** A p. having a regular macroscopic structure, without necessarily showing microcrystallinity Cf. *polyallomers* **orientated ~** A p film that has been stretched mechanically in 2 directions at right angles to improve its strength properties. **redox ~** Electron-exchange p. **regular ~** Tactic p **super ~** A p in which the polymerized molecules have an average molecular weight exceeding 10,000. **tactic ~** A p with only one type of repeating unit See *tacticity*

P.R. Trade name for a polyamide synthetic fiber

polymeric Related molecularly to an isomeric compound, but having a multiple of its molecular weight, as, acetylene and benzene. See *polymerism*. **p. dialdehyde** See *starch dialdehyde*.

polymericular weight The molecular weight of a polymer

polymeride Polymer.

polymerisation Polymerization

polymerism The property of certain organic compounds which have the same percentage composition, but different molecular weights, the heavier being multiples of the lighter

EXHIBIT 12

REDACTED IN ITS ENTIRETY